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Trial participation disclosure and gel use behavior in the CAPRISA 004 tenofovir gel trial

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Disclosure, or open communication, by female microbicide trial participants of their trial participation and use of an investigational HIV prevention drug to a sexual partner may affect participants' trial product usage behavior and contribute to poor adherence. With mixed results from recent microbicide clinical trials being linked to differing participant adherence, insights into the communication dynamics between trial participants and their sexual partners are particularly important. We examined the quantitative association between (1) communication of trial participation to a partner and participant adherence to gel and (2) communication of trial participation to a partner and participant HIV status. An in-depth adherence and product acceptability assessment was administered to the women participating in the CAPRISA 004 trial. Additionally, we collected qualitative data related to communication of trial participation and gel use. Qualitatively, among 165 women who had reported that they had discussed trial participation with others, most (68%) stated that they communicated participation to their sexual partner. Most of the women who had communicated study participation with their partners had received a positive/neutral response from their partner. Some of these women stated that gel use was easy; only a small number said that gel use was difficult. Among women who did not communicate their study participation to their partners, difficulty with gel use was more common and some women stated that they feared communicating their participation. Quantitatively, there was no statistically significant difference in the proportions of women who had communicated study participation to a partner across different adherence levels or HIV status. A deeper knowledge of the dynamics surrounding trial participation communication to male partners will be critical to understanding the spectrum of trial product usage behavior, and ultimately to designing tailored strategies to assist trial participants with product adherence.

Keywords: vaginal microbicide; HIV prevention; disclosure; adherence; covert use; partner dynamics

Introduction

Previous microbicide, diaphragm, and condom studies and clinical trials have explored barriers women face in disclosing, or openly communicating, study or trial participation to sexual partners including fear of violating trust or relationship norms, partners' refusal of study product use, and physical violence (Gafos et al., 2012; Montgomery et al., 2008; Montgomery, Gafos et al., 2010; Montgomery, Cheng et al., 2010; Morrow et al., 2003; Sahin-Hodoglugil et al., 2006; Sahin-Hodoglugil et al., 2011; Woodsong & Alleman, 2008; Woodsong et al., 2013). Studies have also explored linkages between communication of participation and study product adherence and found more consistent usage among women whose partners knew of their participation (Greene et al., 2010; Montgomery et al., 2008; Montgomery, Gafos et al., 2010; Montgomery, Cheng et al., 2010; Pistorius et al., 2004; van der Straten et al., 2008; Woodsong & Alleman, 2008). One study showed product adherence was more difficult for women whose partners were not aware of their participation and product use (Sahin-Hodoglugil et al., 2006).

Study product adherence has been cited as an important factor in the mixed results seen in recent antiretroviral (ARV)-based microbicide and HIV prevention trials. The 2010 CAPRISA 004 tenofovir gel microbicide trial in South Africa demonstrated a 39% reduction in HIV infections; in secondary analyses, infections were reduced by 54% among women with high adherence to the study product (Abdool Karim et al., 2010). Similar dose–response effects have been observed in other HIV prevention trials including iPrEx (Grant et al., 2010), PartnersPrep (Baeten et al., 2012), and TDF2 (Thigpen et al., 2011). In contrast, two studies with evidence of poor adherence were unable to demonstrate product effectiveness (Marrazzo, Ramjee, & Nair, 2013; Van Damme et al., 2012).

We used a mixed methods approach to explore the relationships between communication of participation in the CAPRISA 004 microbicide trial to male sexual partners, participant HIV status, and use of study product.

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Methods

The study was approved by FHI 360's Protection of Human Subjects Committee in Durham, NC, USA and the University of KwaZulu-Natal Biomedical Research Ethics Committee in Durban, South Africa.

Study population

This study was conducted simultaneously with the CAPRISA 004 microbicide gel clinical trial in KwaZulu-Natal, South Africa. Participants (n = 277) were recruited from the CAPRISA 004 study population (n = 889). All trial participants with a positive HIV test result at their monthly clinic visit were targeted for recruitment[1] and 72 confirmed positive were enrolled. Trial participants with negative HIV test results were selected randomly (n = 205). Demographics and sexual behavior were similar to the larger CAPRISA 004 cohort. A detailed description of the study design has been published elsewhere (MacQueen et al., 2014).

All participants previously met CAPRISA 004 trial eligibility criteria (aged 18–40 years, sexually active, HIV-negative at enrollment, not pregnant, and using a non-barrier form of contraception). Additionally, women had to be enrolled in the trial for a minimum of two months and not be suspended from gel use for three months prior to their most recent HIV test.

Data collection

A one-time, face-to-face in-depth adherence and gel acceptability assessment was conducted with participants in the local language, isiZulu. Topics covered included:

- general feelings about trial participation;
- gel and condom use patterns and challenges;
- communication with others about the trial;
- community perceptions about the trial; and
- beliefs about the gel.

The Timeline Followback (TLFB) method (Carey, Carey, Maisto, Gordon, & Weinhardt, 2001) was used to measure gel usage over a three-month recall period. Adherence was measured by the proportion of vaginal sex events covered by the prescribed dosage of gel with 0–50% events covered categorized as low, 51–80% as moderate, and 81–100% as high. Prescribed dosage was one dose within 12 hours before sex, one dose within 12 hours after sex, and no more than two doses in 24 hours (Abdool Karim et al., 2010). Recorded interviews were transcribed by native isiZulu speakers using a standardized transcription protocol (McLellan-Lemal, 2008) then translated into English. To reduce bias, measures were taken to prevent interviewers from knowing participants' HIV status. However, 10 participants (with positive HIV test results) divulged their HIV test results during the interview.

Data analysis

Logistic regression was used to assess the association between communication of trial participation to a partner and (1) participant adherence to gel and (2) participant HIV status.

Qualitative data were coded using a team-based, data-driven, thematic approach and implemented with AnSWR qualitative data analysis software. Two coders separately coded 20% of transcripts and inter-coder agreement checks were conducted. Discrepancies in coding were resolved to ensure a minimum of 80% agreement. Code frequencies and co-occurrences were examined for trends related to trial participation communication, ease of gel use, and partner's reaction to communication of trial participation.

Results

Quantitative findings

Participant demographics and baseline sexual behavior data are shown in Table 1. Logistic regression analyses examining the degree to which communication with a partner predicted adherence level or HIV status failed to reveal any statistically significant associations (Table 2).

Qualitative findings

In total, 165 (60%) participants discussed communication of trial participation during their interview. Of these, most (68%) stated that they had communicated participation in the trial to at least one sexual partner. A majority of the communicators (n = 74, 65%) said their partners responded positively or neutrally. Some (n = 23) said gel use was easy; only seven described gel use as difficult. Women reporting positive or neutral partners mentioned the ease of being able to insert gel in their partner's presence and ability to use gel when their partner visited unexpectedly. Some women said their partners facilitated use by providing reminders for gel insertion before and after sex and for trial-related appointments:

> *Interviewer:* Ok, is it difficult to remember to insert the gel?
> *Respondent:* No, it's not difficult … Because anyway I keep my gel where we sleep, then he also reminds me because he is not someone with a good behavior so that I get protected from getting the disease.

Of the 165 women who discussed trial participation communication, 52 (32%) did not communicate trial

Table 1. Participant demographics and baseline sexual behavior.

Variable	HIV+ participants (n = 72)	HIV– participants (n = 205)
Demographic characteristics		
Mean age (years)	22.7	24.2
Monthly income <R1000 (R = South African Rand)	76.3%	83.4%
Married	2.7%	6.3%
Stable partner	94.4%	89.2%
Sexual behavior at baseline		
Mean age at sexual debut (years)	17.1	17.4
Mean number sexual partners (lifetime)	2.9	3.0
Mean age of oldest partner (years, past 30 days)	26.0	27.9
Reported sex in the past 7 days	54.1%	62.4%
Always use condom during sex	33.3%	32.6%
New partner (past 30 days)	0.0%	1.4%
Anal sex (past 30 days)	0.0%	0.4%

participation to any partner. One-third of non-communicators said that gel use was hard and more than 20% said they were afraid to communicate. Non-communicators said they were often unable to use gel when their partner was present or when their partner visited unexpectedly:

> *Interviewer:* What maybe made you not use the gel even when you had sex?
> *Respondent:* At other times it's because you think this person isn't coming, you see, all of a sudden, you see him arriving, then it's not easy for me to insert this thing because he doesn't know that I am using this gel.

They also expressed concern that they would be unable to hide the product and feared their partner would feel the cold and wetness of the gel, which may cause arguments or accusations of cheating. Furthermore, some said that communication of trial participation would incite anger from or lead to abandonment by their partners or that their partners may prohibit gel use:

> *Respondent:* One time my boyfriend asked me "why am I feeling something water-like in your vagina? Do you maybe have any disease or you have slept with someone else? I said, 'no, I don't have anything'." Then he was a bit angry.
> *Interviewer:* Why are you not telling him that you are using the gel?
> *Respondent:* No, he would be angry and tell me to stop.

Two additional themes emerged among women who did not communicate trial participation to any partner: (1) fear that communication would lead to their partner no longer using condoms and (2) partial communication of trial participation. The latter was discussed in two ways: some women communicated their participation in a

Table 2. Results of regression analyses.

Adherence level regressed on communication with a partner

		Adherence level			Cumulative logistic regression
Communication with partner	Participants (n = 271)	Low	Moderate	High	OR Lower → higher
No	63 (23%)	14%	33%	52%	1.04
Yes	208 (77%)	14%	35%	51%	[95% CI: 0.606, 1.783]

HIV status regressed on communication with a partner

		HIV		Logistic regression
Communication with partner	Participants (n = 277)	No	Yes	OR
No	67 (24%)	73%	27%	0.94
Yes	210 (76%)	74%	26%	[95% CI: 0.506, 1.756]

clinical trial, but did not specify they were inserting a microbicide into their vagina, while other women revealed to their partner that they were participating in a trial that involved gel use, but did not specify the gel was being studied for HIV prevention:

> *Respondent:* I told him that I am cleaning my bladder, I didn't tell him it's [the gel] purpose.

Discussion

The results described here add to the body of knowledge around partner communication in the context of an HIV prevention clinical trial and provide important insights into women's successes and challenges adhering to microbicide gel. In the high HIV prevalence setting of KwaZulu-Natal, South Africa, the majority of study participants communicated to their sexual partners that they were taking part in a microbicide trial. The qualitative data showed that an important minority of participants did not communicate their study participation to their sexual partner(s), and many of these women also reported difficulties with gel use. We did not find a statistically significant association between communication of trial participation and either study product adherence or HIV status. However, an analysis of data from all participants interviewed when exiting the CAPRISA 004 trial found a statistically significant though moderate relationship between disclosure and adherence; no relationship was found between disclosure and either HIV incidence or gel efficacy (Mngadi et al., 2014). Given the moderate association with adherence, it is possible that our sample size was too small to detect a relationship, or that it was obscured by biases in the self-report measures we used.

This study adds to existing evidence concerning the important role that communication between partners can play in supporting the use of products like tenofovir gel to reduce HIV acquisition in women. Just as importantly, it highlights the importance of finding ways to support product adherence among women who are not able to communicate effectively with their partners about HIV prevention. No single product adherence strategy can be applied to all HIV prevention trials or product introduction campaigns. Guidance is needed to inform adherence strategies that both involve male partners of those women who want to communicate their study participation and that support women who would like to use a study product without their partner's knowledge. Moving forward, we must continue to monitor how communication dynamics with partners influence trial participants' ability to adhere to microbicides and other new HIV prevention technologies like PrEP.

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Note

1. For more details about a description of the HIV testing algorithm, see Abdool Karim et al. (2010).

References

Abdool Karim, Q., Abdool Karim, S. S., Frohlich, J. A., Grobler, A. C., Baxter, C., Mansoor, L. E., … Taylor, D. (2010). Effectiveness and safety of tenofovir gel, an antiretroviral microbicide, for the prevention of HIV infection in women. *Science*, *329*, 1168–1174. doi:10.1126/science.1193748

Baeten, J. M., Donnell, D., Ndase, P., Mugo, N. R., Campbell, J. D., Wangisi, J., … Celum, C. (2012). Antiretroviral prophylaxis for HIV prevention in heterosexual men and women. *New England Journal of Medicine*, *367*, 399–410.

Carey, M. P., Carey, K., Maisto, S., Gordon, C., & Weinhardt, L. (2001). Assessing sexual risk behaviour with the Timeline Followback (TLFB) approach: Continued development and psychometric evaluation with psychiatric outpatients. *International Journal of STD & AIDS*, *12*, 365–375. doi:10.1258/0956462011923309

Gafos, M., Mzimela, M., Ndlovu, H., Pool, R., Elford, J., & the MDP Team. (2012). *What have men got to do with it?: The role of men in reproductive and sexual health in a predominantly rural area of KwaZulu-Natal, South Africa*. Paper presented at the 2012 International Microbicides Conference, Sydney, Australia.

Grant, R. M., Lama, J. R., Anderson, P. L., McMahan, V., Liu, A. Y., Vargas, L., … Glidden, D. V. (2010). Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. *New England Journal of Medicine*, *363*, 2587–2599. doi:10.1056/NEJMoa1011205

Greene, E., Batona, G., Hallad, J., Johnson, S., Neema, S., & Tolley, E. E. (2010). Acceptability and adherence of a candidate microbicide gel among high-risk women in Africa and India. *Culture, Health & Sexuality*, *12*, 739–754. doi:10.1080/13691051003728599

MacQueen, K. M., Weaver, M. A., van Loggerenberg, F., Succop, S., Majola, N., Taylor, D., … Karim, S. A. (2014). Assessing adherence in the CAPRISA 004 tenofovir gel HIV prevention trial: Results of a nested case–control study. *AIDS and Behavior*, *18*, 826–832. doi:10.1007/s10461-014-0753-8

Marrazzo, J., Ramjee, G., & Nair, G. (2013). *Pre-exposure prophylaxis for HIV in women: Daily oral tenofovir, oral tenofovir/emtricitabine or vaginal tenofovir gel in the VOICE study (MTN 003)*. Paper presented at the 20th

Conference on Retroviruses and Opportunistic Infections, Atlanta, GA.

McLellan-Lemal, E. (2008). Transcribing data for team-based research. In G. Guest & K. M. MacQueen (Eds.), *Handbook for team-based qualitative research* (p. 101). Lanham, MD: Altamira Pr.

Mngadi, K. T., Maarschalk, S., Grobler, A. C., Mansoor, L. E., Frohlich, J. A., Madlala, B., … Karim, Q. A. (2014). Disclosure of microbicide gel use to sexual partners: Influence on adherence in the CAPRISA 004 trial. *AIDS and Behavior*, *18*, 849–854. doi:10.1007/s10461-014-0696-0

Montgomery, C. M., Gafos, M., Lees, S., Morar, N. S., Mweemba, O., Ssali, A., … Team, T. M. (2010). Reframing microbicide acceptability: Findings from the MDP301 trial. *Culture, Health & Sexuality*, *12*, 649–662. doi:10.1080/13691051003736261

Montgomery, C. M., Lees, S., Stadler, J., Morar, N. S., Ssali, A., Mwanza, B., … Pool, R. (2008). The role of partnership dynamics in determining the acceptability of condoms and microbicides. *AIDS Care*, *20*, 733–740. doi:10.1080/09540120701693974

Montgomery, E. T., Cheng, H., van der Straten, A., Chidanyika, A. C., Lince, N., Blanchard, K., … Padian, N. S. (2010). Acceptability and use of the diaphragm and Replens® lubricant gel for HIV prevention in Southern Africa. *AIDS and Behavior*, *14*, 629–638. doi:10.1007/s10461-009-9609-z

Morrow, K., Rosen, R., Richter, L., Emans, A., Forbes, A., Day, J., … Kelly, C. (2003). The acceptability of an investigational vaginal microbicide, PRO 2000 Gel, among women in a phase I clinical trial. *Journal of Women's Health*, *12*, 655–666. doi:10.1089/154099903322404302

Pistorius, A., van de Wijgert, J., Sebola, M., Friedland, B., Nagel, E., Bokaba, C., & Hoosen, A. (2004). Microbicide trials for preventing HIV/AIDS in South Africa: Phase II trial participants' experiences and psychological needs. *SAHARA-J: Journal of Social Aspects of HIV/AIDS Research Alliance*, *1*(2), 78–86. doi:10.1080/17290376.2004.9724830

Sahin-Hodoglugil, N. N., Montgomery, E., Kacanek, D., Morar, N., Mtetwa, S., Nkala, B., … van der Straten, A. (2011). User experiences and acceptability attributes of the diaphragm and lubricant gel in an HIV prevention trial in southern Africa. *AIDS Care*, *23*, 1026–1034.

Sahin-Hodoglugil, N. N., van der Straten, A., Cheng, H., Montgomery, E. T., Kacanek, D., Mtetwa, S., … Padian, N. (2006). Degrees of disclosure: A study of women's covert use of the diaphragm in an HIV prevention trial in sub-Saharan Africa. *Social Science & Medicine*, *69*, 1547–1555. doi:10.1016/j.socscimed.2009.08.014

Thigpen, M., Kebaabetswe, P., Smith, D., Segolodi, T., Soud, F., Chillag, K., & Paxton, L. (2011). *Daily oral antiretroviral use for the prevention of HIV infection in heterosexually active young adults in Botswana: Results from the TDF2 study*. Paper presented at the 6th IAS Conference on HIV Pathogenesis, Treatment and Prevention, Rome.

Van Damme, L., Corneli, A., Ahmed, K., Agot, K., Lombaard, J., Kapiga, S., … Taylor, D. (2012). *The FEM-PrEP trial of emtricitabine/tenofovir disoproxil fumarate (Truvada) among African women*. Paper presented at the 19th Conference on Retroviruses and Opportunistic Infections, Seattle.

van der Straten, A., Moore, J., Napierala, S., Clouse, K., Mauck, C., Hammond, N., & Padian, N. (2008). Consistent use of a combination product versus a single product in a safety trial of the diaphragm and microbicide in Harare, Zimbabwe. *Contraception*, *77*, 435–443. doi:10.1016/j.contraception.2008.02.013

Woodsong, C., & Alleman, P. (2008). Sexual pleasure, gender power and microbicide acceptability in Zimbabwe and Malawi. *AIDS Education & Prevention*, *20*, 171–187. doi:10.1521/aeap.2008.20.2.171

Woodsong, C., MacQueen, K., Amico, K. R., Friedland, B., Gafos, M., Mansoor, L., … McCormack, S. (2013). Microbicide clinical trial adherence: Insights for introduction. *Journal of the International AIDS Society*, *16*(1), 18505. doi:10.7448/IAS.16.1.18505